PATENT SPECIFICATION

NO DRAWINGS

Inventor: HENRY C. BURNS

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International Classification: —A 61 k 19/00

COMPLETE SPECIFICATION

Wound Debriding and Healing Composition

We, BURNS PHARMACEUTICALS, INC., of 7711 Oakport Street, Oakland, State of California, United States of America, a corporation organized under the laws of the State of

SPECIFICATION NO. 1,161,192

By a direction given under Section 17 (1) of the Patents Act 1949 this application proceeded in the name of BURNS PHARMACEUTICALS INC., formerly BURNS SERVICE CORPORATION, a Corporation organized under the laws of the State of California, United States of America of 7711 Oakport Street, Oakland, State of California, United States of America.

THE PATENT OFFICE

R 123488/4

relieve pain, debride necrotic tissue, stimulate tissue repair by normal epithelial granulation, control excessive tissure granulation and to reduce the malodorous effect of dead tissue.

According to the present invention there is provided a composition for increasing the rate of wound healing which comprises Castor Oil, Balsam Peru, and Trypsin. The composition is preferably in liquid areosol form.

Unlike other proteolytic products which often exhibit a non-discriminating activity (attacking viable as well as necrotic tissue) and lack the disbursing and penetrating capabilities, the present composition disburses rapidly, uniformly and completely over the entire wound surface, penetrates deeply into the cellular interstitial spaces and debrides only dead or dying tissue to a maximum degree in the minimum time; stimulates optimum growth of new cells from the remaining healthy tissue; inhibits the proliferation of connective tissue thus reducing scar tissue formation; and remarkably and unexpectedly stops cell regeneration when the need for such granulation ceases (wound is healed) thus preventing exuberant (excessive) granulation, which is often an unfavourable result with [illegible]

combination.

The administration to wounds of animal and man of a composition, consisting of Trypsin, Balsam Peru and Castor Oil and Igepal when emulsified and formulated to produce a foaming, which disburses uniformly, penetrates the tissues and produces significant results in debriding dead cells, organic debris, bacterial decay; controlling excessive granulation; stimulating normal healthy tissue regeneration; promoting optimum wound healing; and treating ulcers, lacerations, abrasions, abscesses, otitis, penetrating wounds, fistulas, burns, necrotic dermatoses, vaginitis, pyometra, etc. Further the preferable composition according to the invention provides a protective water miscible coating which permits oxygen entry for wound breathing and prevents infective organism entry; there is control of pain and minimal scarring.

These unusual and seemingly opposing actions of debriding necrotic tissue and wound healing have been tested in the United States of America. The results have been substan-

SPECIFICATION AMENDED - SEE ATTACHED SLIP

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COMPLETE SPECIFICATION

Wound Debriding and Healing Composition

We, BURNS PHARMACEUTICALS, INC., of 7711 Oakport Street, Oakland, State of California, United States of America, a corporation organised under the laws of the State of California, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement: —

This invention relates to a homogeneous pharmaceutical formulation for topical and body cavity administration in humans and animals which is designed to promote healing of lacerations, abscesses, otitis, burns, ulcers, and aberations of the skin and epithelium, relieve pain, debride necrotic tissue, stimulate tissue repair by normal epithelial granulation, control excessive tissure granulation and to reduce the malodorous effect of dead tissue.

According to the present invention there is provided a composition for increasing the rate of wound healing which comprises Castor Oil, Balsam Peru, and Trypsin. The composition is preferably in liquid areosol form.

Unlike other proteolytic products which often exhibit a non-discriminating activity (attacking viable as well as necrotic tissue) and lack the disbursing and penetrating capabilities, the present composition disburses rapidly, uniformly and completely over the entire wound surface, penetrates deeply into the cellular interstitial spaces and debrides only dead or dying tissue to a maximum degree in the minimum time; stimulates optimum growth of new cells from the remaining healthy tissue; inhibits the proliferation of connective tissue thus reducing scar tissue formation; and remarkably and unexpectedly stops cell regeneration when the need for such granulation ceases (wound is healed) thus preventing exuberant (excessive) granulation, which is often an unfavourable result with such wound treatments.

The composition of the invention produces more controlled healing because it exercises a unique selective capability of both stimulating a rapid regeneration of normal cell proliferation when needed to "fill in" a wound damage, yet inhibits and prevents an excessive cell growth and exuberant granulation when the need to "fill in" has been satisfied. While the combination of Trypsin, Balsam Peru and Castor Oil in a liquid aerosol form is highly advantageous, further advantages to be gained if Igepal and Isopropanol are added to this combination.

The administration to wounds of animal and man of a composition, consisting of Trypsin, Balsam Peru and Castor Oil and Igepal when emulsified and formulated to produce a foaming, which disburses uniformly, penetrates the tissues and produces significant results in debriding dead cells, organic debris, bacterial decay; controlling excessive granulation; stimulating normal healthy tissue regeneration; promoting optimum wound healing; and treating ulcers, lacerations, abrasions, abscesses, otitis, penetrating wounds, fistulas, burns, necrotic dermatoses, vaginitis, pyometra, etc. Further the preferable composition according to the invention provides a protective water miscible coating which permits oxygen entry for wound breathing and prevents infective organism entry; there is control of pain and minimal scarring.

These unusual and seemingly opposing actions of debriding necrotic tissue and wound healing have been tested in the United States of America. The results have been substan-

tiated by fifty independent investigators in the United States of America whose clinical responses were reported to the United States Department of Health, Education and Welfare which granted new drug approval.

The fifty investigators after administering a total of approximately 16,000 doses to horses, cattle and small animals reported good or excellent healing results in 97% of the treated animals; good or excellent results in debridement in 95% of the cases; good or excellent results in 97% for tissue repair; good or excellent results in 59% for deodorant characteristics; good or excellent results for pain reduction and good or excellent results in controlling excessive granulation in 77% of the animals treated.

The composition of this invention may be administered by spraying from an aerosol container from a distance of approximately 6 inches from the area to be treated. For the treatment of deep puncture wounds; abscesses, fistulas, otitis, and anal gland infections, and body cavities such as vagina; a separate nozzle and plastic tube can be inserted and sprayed into the heart of the abscess or wound to permit complete dissolution and discharge of the pus and debris interfering with normal healing. The use of the aerosol not only eliminates the need for messy ointments, powders and liquids but due to foaming causes the composition to distribute itself and penetrate the tissues to a far greater degree. A preferred formulation of the composition of the present invention which demonstrates the remarkable foaming action when dispensed from an aerosol can is as follows:

	mg. per Gm.
Castor Oil	550.0
Balsam Peru	72.5
Trypsin	0.1
Isopropanal	327.25
Igepal CO-530	50.0

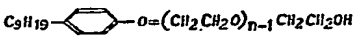
In this formulation, the Balsam Peru is mixed with the Castor Oil and Isopropanol. The Trypsin is triturated with the Igepal CO-530 and added to the mixture. The resulting suspension is filtered and filled into the aerosol containers. Each aerosol container contains approximately 70% of the above suspension and 30% Dichlorodifluoromethane as the propellant.

One or more of the active ingredients i.e. Castor Oil, Balsam Peru and Trypsin may vary in a particular formulation by 50% from the proportions set forth in the above preferred example and still provide efficacy. In like manner, the Isopropanol and Igepal CO-530 may vary by 50% from the proportions in the optimum example, to produce emulsification and foaming.

Other proportions which are suitable for the composition of the present invention are:

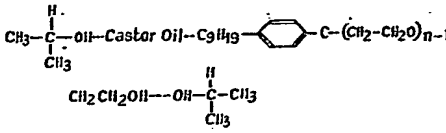
275 to 825 mg. per Gm. of Castor Oil;
36.20 to 108.7 mg. per Gm. of Balsam Peru;
.05 to .15 mg. per Gm. of Trypsin;
163.5 to 490.75 mg. per Gm. of Isopropanol; and
25 to 75 mg. per Gm. of Igepal CO-530.

To initiate rapid therapeutic effect it is well known that wetting is a vital pre-requisite in percutaneous absorption and topical drug therapy. A further problem is the difficulty in getting Balsam Peru which is a heavy resin out of the can and distributed over the wound so as to obtain maximum penetration of the tissues. These criteria have been met by the coaction of Igepal CO-530 and Isopropyl alcohol with the active ingredients. Igepal CO-530 is a non-ionic surface acting agent, chemically known as nonylphenpoly (ethyleneoxy) ethanol, with the following formula:



"n" denotes the number of moles of ethylene oxide per mole of nonylphenol, and for Igepal CO-530 "n" has a value of 6.

The unique foaming action may be explained by the pyhsio-chemical interactions of Igepal CO-530 to Isopropyl Alcohol and Castor Oil in the presence of air when the spray is delivered upon the open or wounded area. Inside the container, the surface acting Igepal interacts with Castor Oil and Isopropyl Alcohol through hydrogen bonding and Van der Waals forces providing an emulsion as



There are many actions of Igepal: Initial wetting of Castor Oil, Isopropyl Alcohol; deflucculation and suspension of Trypsin and Balsam Peru; solubilization of Castor Oil and Isopropyl Alcohol. Upon spraying, the surfactant solution produces relatively stable foams when intimately mixed with air. The foam gradually dissipates as the liquid drains into the affected area surrounding the air globules and the film finally collapses. The end result is to reduce surface and interfacial tensions giving rise to adsorption and spreading. The penetration of Trypsin and other ingredients is therefore increased by the presence of Igepal, providing maximum efficiency as well as unique selectivity of Trypsin as formulated for dead tissue only.

Examples I and II below demonstrate the usefulness of the composition of the invention in the acceleration of the healing of various types of wounds in animals.

EXAMPLE I

Species: Equine; Sex: Male; Age: Six (6) years; Weight: 1100 lbs.

History: This animal had been in pasture all night and severely lacerated the anterior surface of the right knee. The entire surface of the knee was pulled back, exposing the subcutaneous tissue for an area of 3 inches from the margin of the laceration. The wound was 3—6 hours old when seen for the first time. The wound was stitched using a synthetic, nonabsorbable suture. The edges were approximated using retention sutures (short pieces of rubber tubing) to minimize the cutting out of the sutures. A pressure dressing was applied from the pastern to an area 6 inches above the knee and changed every 3 days. The animal received penicillin and streptomycin daily for 5 days and a tetanus toxoid injection was given. After 10 days the sutures were removed and the leg redressed for another 10 days. The dressing was removed and the laceration had healed by primary intention. However, there were several areas where exuberant granulation had developed and this required further treatment. The composition of the invention was applied to these areas without further surgical treatment. The regimen consisted of two applications daily for 14 days. Using this technique the granulation ceased to be a problem in an area that is usually very difficult to heal.

The composition of the invention was extremely effective in controlling the problem of granulation in this case. The results were excellent and the horse was back on the track in 35 days after the initial laceration. Six months is the usual healing time for this type of laceration.

EXAMPLE II

Cat with neglected multiple abscesses and fistulas which discharged and produced extensive skin necrosis, bacterial invasion, and heavy pustular exudation. The composition of this invention was sprayed 2 times daily without any supportive treatment (antibiotics, steroids, etc.) which might interfere with rapidity of healing, regeneration of skin, and minimal scarring. There was complete healing within 8 weeks, and almost total absence of scar tissue and a remarkable regeneration of normal skin with regrowth of hair.

The precise explanation of the synergistic, selective, bacteriostatic, regenerating, debriding, scar-inhibiting, and stimulating actions on wounds of the inventive composition is unknown. However, preferred composition of the invention creates a unique foaming action which distributes the three active ingredients (Castor Oil, Balsam Peru and Trypsin) and provides maximum penetration of the tissues and deposition. Deposition of the Trypsin into the deepest portions allows it to remove all the dead material. Removal of all the dead material in the deepest portions of the wound prevents continued festering and delayed healing. The Trypsin dissolves the dead material and creates an effervescence which foams up and spreads out immediately in an even distribution. The foam lasts only about 30 seconds which gives the composition its effectiveness.

The spreading and penetration of the Trypsin and Balsam Peru are two major achievements; particularly the Balsam Peru which is a hard resin and difficult to spread and cause to penetrate into the wound. Another action present is the agitation of the resin which creates a mixing of the composition which further assists the spreading and penetration.

When the Trypsin dissolves the debrided tissue it comes immediately to the surface. The cells themselves exude liquids which push the dead material to the surface.

The Castor Oil stimulates new cells to form and the Balsam Peru acts as a protectant against external debris by forming a coating. The result of this unique combination of medicaments is a specific design which produces five times faster healing than any other wound treatment.

WHAT WE CLAIM IS:—

1. A composition for increasing the rate of wound healing which comprises Castor Oil, Balsam Peru and Trypsin.

2. A composition as claimed in claim 1, in liquid aerosol form.

3. A composition as claimed in claim 1, including Isopropanol and Igepal CO-530.

4. A composition useful for increasing the rate of wound healing which comprises: 275 to 825 mg. per Gm. of Castor Oil; 36.20 to 108.7 mg. per Gm. of Balsam Peru; and .05 to .15 mg. per Gm. of Trypsin.

5. A composition as claimed in claim 4, including 163.5 to 490.75 mg. per Gm. of Isopropanol; and 25 to 75 mg. per Gm. of Igepal CO-530 in a liquid aerosol form mixed to form a suspension.

6. A composition as claimed in claim 5, wherein the resulting suspension is filtered and filled into aerosol containers, each container containing approximately 70% of the said suspension and approximately 30% Dichlorodifluoromethane as the propellant.

7. A method of treating wounds in non-human animals which consists in administering the combination of Castor Oil, Balsam Peru and Trypsin.

8. A method of treating wounds in non-human animals which consists in administering the combination of Castor Oil, Balsam Peru and Trypsin in liquid aerosol form.

9. A method of treating wounds in non-human animals which consists in administering the combination of Castor Oil, Balsam

Peru, Trypsin, Isopropanol and Igepal CO-530.

10. A method as claimed in Claim 7, wherein the combination comprises Castor Oil in the amount of 275 to 825 mg. per Gm; Balsam Peru in the amount 36.2 to 108.7 mg. per Gm.; and Trypsin in the amount .05 to .15 mg per Gm.

11. A method as claimed in claim 9, wherein the combination comprises Castor Oil in the amount of 275 to 825 mg. per Gm; Balsam Peru in the amount 36.2 to 108.7 mg. per Gm; Trypsin in the amount .05 to .15 mg. per Gm.; Isopropanol in the amount 163.5 to 490.75 mg. per Gm. and Igepal CO-530 in the amount 25 to 75 mg. per Gm.

12. A composition useful for increasing the rate of wound healing substantially as herein described.

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